In the Claims

Please amend the claims presented during the international phase as follows. Applicant presents a full set of claims showing markups of the claims with insertions and deletions indicated by underlining and strikethrough text (or double bracketing), respectively.

1. (Original) A method of detecting an enzyme in a sample, which enzyme is capable of adding or removing a chemical moiety to or from a nucleic acid molecule, thereby conferring altered sensitivity of the nucleic acid molecule in a subsequent process, the method comprising:

- allowing the sample to be tested for the presence of the enzyme to interact with the nucleic acid molecule; and
- testing for interaction of the enzyme with the nucleic acid molecule by detecting the altered sensitivity of the nucleic acid molecule caused by the enzyme.

2. (Original) A method according to claim 1 wherein the enzyme is a phosphatase capable of removing terminal phosphates from a nucleic acid molecule.

3. (Currently amended) A method according to claim 1 ~~or 2~~ wherein the enzyme is alkaline phosphatase.

4. (Original) A method according to claim 3 wherein the alkaline phosphatase is any of serum alkaline phosphatase, calf intestinal phosphatase (CIP), bacterial alkaline phosphatase (BAP) or shrimp alkaline phosphatase.

5. (Currently amended) A method according to claim 1 ~~or 2~~ wherein the enzyme being detected is prostatic acid phosphatase.

6. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 5~~ wherein the altered sensitivity of the nucleic acid molecule that is detected is protection of the nucleic acid molecule from nuclease digestion.

7. (Original) A method according to claim 6 wherein the detection step is carried out by incubating the sample with nuclease enzymes and testing for the presence or absence of the nucleic acid molecule following incubation with nuclease enzymes.

8. (Currently amended) A method according to claim 6 ~~or 7~~ wherein the nuclease used to distinguish between nucleic acid molecules whose sensitivity in a subsequent process has been changed by enzyme activity in the sample and those whose sensitivity has not by digesting unchanged nucleic acid molecules comprises an exonuclease or both an endonuclease and an exonuclease or two complementary exonucleases.

9. (Original) A method according to claim 8 wherein the exonuclease used is lambda exonuclease.

10. (Original) A method according to claim 9 wherein the complementary exonuclease used is exonuclease I or the endonuclease used is mung bean endonuclease.

11. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 10~~ wherein the nucleic acid molecule is blunt ended.

12. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 11~~ wherein the nucleic acid molecule comprises dsDNA.

13. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 12~~ wherein the nucleic acid molecule is phosphorylated at both 5' ends.

14. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 12~~ wherein the nucleic acid molecule is phosphorylated at a single 5' end.

15. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 14~~ wherein the nucleic acid molecule is produced by a DNA amplification technique using phosphorylated primers.

16. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 15~~ wherein the nucleic acid is treated with a kinase enzyme.

17. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 16~~ wherein the nucleic acid molecule is produced from a plasmid.

18. (Original) A method according to claim 17 wherein the plasmid comprises one of pUC derivatives and pBR322.

19. (Currently amended) A method according to claim 17 ~~or 18~~ wherein the plasmid is cleaved using restriction enzymes to produce blunt ended linear nucleic acid molecule(s).

20. (Original) A method according to claim 1 for detection of a phosphatase comprising the substeps of:

a) adding to the sample a nucleic acid molecule which comprises blunt ended dsDNA which is phosphorylated at one 5' end only

b) incubating under conditions which permit phosphatase activity

c) adding lambda exonuclease and mung bean endonuclease or exonuclease I to the sample and allowing incubation with these enzymes; and

d) detecting the altered sensitivity of the nucleic acid molecule, measured as the presence or absence of the nucleic acid molecule.

21. (Currently amended) A method according to claim 10 ~~any one of claims 10 to 20~~ wherein the mung bean endonuclease or exonuclease I is at a concentration low enough to substantially prevent dsDNA digestion activity.

22. (Original) A method according to claim 1 for detection of a phosphatase comprising the substeps of:

a) adding to the sample a nucleic acid molecule which comprises blunt ended dsDNA which is phosphorylated at both 5' ends

b) incubating under conditions which permit phosphatase activity

c) adding lambda exonuclease to the sample and allowing incubation with this enzyme; and

d) detecting the altered sensitivity of the nucleic acid molecule, measured as the presence or absence of the nucleic acid molecule.

23. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 22~~ wherein the altered sensitivity of the nucleic acid molecule is detected using nucleic acid amplification techniques.

24. (Original) A method according to claim 23 wherein the nucleic acid amplification technique used is selected from PCR, Rolling Circle Amplification, NASBA, 3SR and TMA.

25. (Currently amended) A method according to claim 23 ~~or 24~~ wherein the products of amplification are detected using real-time techniques.

26. (Original) A method according to claim 25 wherein the real-time technique consists of any one of Taqman® system, Molecular beacons system and Scorpion probe system.

27. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 26~~ wherein the enzyme is one which is used for detection of an antigen/analyte in an immunoassay.

28. (Original) A method according to claim 27 wherein the enzyme is attached, either directly or indirectly, to an antibody which is used in detection of an antigen/analyte.

29. (Original) A method according to claim 28 wherein the antibody is a primary antibody.

30. (Original) A method according to claim 28 wherein the antibody is a secondary antibody.

31. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 30~~ wherein the method is carried out in a single tube.

32. (Currently amended) A method according to claim 1 ~~or 2~~ wherein the enzyme being detected is associated with an infectious agent, whereby detection of altered sensitivity of the nucleic acid molecule indicates the presence of the infectious agent.

33. (Original) A method according to claim 32 wherein the infectious agent is Aspergillus or Staphyloccocus species.

34. (Currently amended) A method according to claim 1 ~~any one of claims 1, 32 and 33~~ for detection of a phosphatase enzyme associated with an infectious agent comprising the substeps of:

a) capture and separation of the infectious agent-specific phosphatase via a specific antibody

a) adding to the separated phosphatase a nucleic acid molecule which comprises blunt ended dsDNA which is phosphorylated at both 5' ends

b) incubating under conditions which permit phosphatase activity

c) adding lambda exonuclease to the sample and allowing incubation with this enzyme; and

d) detecting the altered sensitivity of the nucleic acid molecule, measured as the presence or absence of the nucleic acid molecule, whereby detection of altered sensitivity indicates the presence of the infectious agent.

35. (Original) A method of diagnosing prostate cancer in a mammalian subject comprising

- allowing a sample obtained from the subject under test to be tested for the presence of prostatic acid phosphatase (PAP) to interact with a nucleic acid molecule; and
- testing for interaction of PAP with the nucleic acid molecule by detecting the altered sensitivity in the nucleic acid molecule caused by PAP in a downstream process, whereby the presence of prostatic acid phosphatase (PAP) in the sample is taken as an indication that the subject has prostate cancer.

36. (Original) A method of diagnosing a disease associated with elevated serum alkaline phosphatase levels in a mammalian subject comprising

- allowing a sample obtained from the subject to be tested for the presence of serum alkaline phosphatase to interact with a nucleic acid molecule; and
- testing for interaction of serum alkaline phosphatase with the nucleic acid molecule by detecting an altered sensitivity in the nucleic acid molecule caused by serum alkaline phosphatase, whereby the presence of serum alkaline phosphatase in the sample is

taken as an indication that the subject has a disease associated with elevated serum alkaline phosphatase levels.

37. (Original) A method according to claim 36 wherein the method is used to diagnose any one of sepsis, AIDS, malignancies, obstructive biliary diseases, infiltrative liver diseases, sepsis and cholangiocarcinoma.

38. (Currently amended) A method according to claim 35 ~~any one of claims 35 to 37~~ wherein the method is carried out *in vitro*.

39. (Currently amended) A method according to claim 35 ~~any one of claims 35 to 37~~ which further comprises obtaining the sample from the subject.

40. (Currently amended) A method according to claim 35 ~~any of claims 35 to 39~~ wherein the subject is a human.

41. (Original) A kit for detecting an enzyme capable of adding or removing a chemical moiety to or from a nucleic acid molecule, which thereby confers altered sensitivity of the nucleic acid molecule in a subsequent process, comprising:

- a nucleic acid molecule which is capable of being acted upon by the enzyme; and
- means for detecting the altered sensitivity of the nucleic acid molecule in the subsequent process.

42. (Original) A kit according to claim 41 wherein the nucleic acid molecule comprises dsDNA.

43. (Currently amended) A kit according to claim 41 ~~or 42~~ wherein the nucleic acid molecule is blunt ended.

44. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 43~~ wherein the nucleic acid molecule is phosphorylated at one or both 5' ends.

45. (Original) A kit according to claim 41 wherein the nucleic acid molecule comprises a plasmid which can be cut using restriction enzymes to give blunt ended dsDNA which is phosphorylated at both 5' ends.

46. (Original) A kit according to claim 45 wherein the plasmid is a pUC derivative or pBR322.

47. (Currently amended) A kit according to claim 45 ~~or 46~~ further including the restriction enzymes necessary to cut the plasmid.

48. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 47~~ wherein the means for measuring the altered sensitivity of the nucleic acid molecule includes an exonuclease and/or an endonuclease or a complementary exonuclease which digests the nucleic acid molecule if the nucleic acid molecule has not been modified by the enzyme.

49. (Original) A kit according to claim 48 wherein the endonuclease comprises mung bean endonuclease or the complementary exonuclease comprises exonuclease I.

50. (Currently amended) A kit according to claim 48 ~~or 49~~ wherein the exonuclease comprises lambda exonuclease.

51. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 50~~ wherein the enzyme being detected is alkaline phosphatase.

52. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 51~~ wherein the means for measuring the altered sensitivity of the nucleic acid molecule requires nucleic acid amplification.

53. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 52~~ wherein the kit further includes reagents necessary for nucleic acid amplification.

54. (Currently amended) A kit according to claim 52 ~~or 53~~ wherein the nucleic acid amplification step is selected from PCR, NASBA, Rolling circle amplification, 3SR and TMA.

55. (Currently amended) A kit according to claim 52 ~~any one of claims 52 to 54~~ wherein the kit further comprises probes and reagents necessary for real-time detection of nucleic acid amplification products.

56. (Original) A kit according to claim 55 wherein the real-time detection method is selected from Taqman® system, Molecular beacons system and Scorpion probe system.

57. (Currently amended) A kit according to claim 41 ~~any one of claims 41 to 56~~ further comprising an antibody selective for an infectious agent-specific phosphatase.

58. (Original) A kit according to claim 57 wherein the infectious agent is Aspergillus or Staphyloccocus species.